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Routine Laboratory Monitoring for Low-Molecular-Weight Heparin Prophylaxis in Burns? Not So Fast!

To the Editor:

We read with interest the report by Lin et al[1] on the use of a protocol to follow-up anti-Xa levels and adjust prophylactic dose low-molecular-weight heparin (LMWH) dosing to maintain anti-Xa levels between 0.2 and 0.4 U/ml. We agree with the authors in their belief that current venous thromboembolic prophylaxis dosing in patients with severe burns may be inadequate. Several recent reports in the trauma critical care literature have identified similar discrepancies between dose and the desired level of anti-Xa activity.[2,3] However, we are not quite convinced that routine monitoring and titration of our LMWH dose to a specific target are necessarily the correct strategy. Our recent experience with attempting to apply this strategy has quickly reminded us that we must proceed with great caution.

A few months ago, we began checking serum anti-Xa levels 4 hours after subcutaneous administration of LMWH in adults with severe burns (greater than 20% TBSA). If serum anti-Xa levels return to a value less than 0.2 U/ml, each dose of LMWH is increased by 10 mg, and the serum anti-Xa level is rechecked the following day. Consistent with the findings by Lin et al, the standard dose of LMWH for prophylaxis did not seem to be adequate in a large number of patients based on a target anti-Xa level. However, of particular concern was one patient specifically whose anti-Xa level never approached 0.2 U/ml despite reaching a dose as high as 90 mg twice daily. This is the recommended therapeutic dose in an otherwise healthy individual weighing 90 kg for the treatment of a newly diagnosed venous thromboembolism! It seems that Lin et al experienced similar issues as 8 of 38 (21%) never reached their "goal" before discontinuation of therapy. In addition, we would like to point out that although other variables may be at play, both venous thromboembolic events (VTE) in the reported study occurred in patients who achieved an appropriate anti-Xa level.

Right away, these issues bring up four vital questions in our minds. First, is a target of 0.2 to 0.4 U/ml the right target? Second, if this is true, at what point, do we stop increasing the dose when levels are not "adequate"? In other words, is there a safe ceiling for dose adjustment for the purposes of prophylaxis? Third, is the serum anti-Xa level the ideal test to monitor efficacy of LMWH dosing in patients with severe burns? Finally, is there currently enough evidence to support broad application of this dosing regimen for burn patients; are we confident that the clinical benefit outweighs the potential risk?

We agree that current methods of dosing of LMWH for VTE prophylaxis in severely burned and critically ill patients are possibly inadequate because of changes in bioavailability, volume of distribution, and hepatic and renal metabolism. However, the strategy of measuring efficacy of LMWH dosing using anti-Xa level may not be accurate in patients with severe burns. LMWH at "subtarget" level may still provide significant protection against clot formation. Increasing doses to try to reach a target number may only increase bleeding complications beyond clinically acceptable levels while providing very little or no extra benefit. Only a well-designed, large prospective randomized trial specifically in our population will help tease out the true clinical benefit of this technique over the status quo. Until then, we caution against the wide adoption of a LMWH prophylaxis strategy based on anti-Xa levels.

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